remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material;

concentrating the treated liquid material by evaporation and drying; and

recovering GMP by separating it from the resin.

10. (Amended) The process according to claim 9 wherein the step of separating the resin from the treated liquid material is accomplished by filtration or centrifugation and the treated liquid material is dried by spray drying.

12. (Amended) The process according to claim 1, wherein the step of recovering the GMP from the resin is accomplished by washing the resin with demineralized water;

desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse;

washing the resin with demineralized water;

combining the eluate and the washings;

demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and

recovering the GMP as the retentate.

13. (Amended) The process according to claim 12 wherein the basic aqueous solution comprises NaOH, KOH or $Ca(OH)_2$, in a concentration of less than 8%.

Please add the following new claim:

23. (New) The process according to claim 12, further comprising the step of freeze-drying the retentate.

## REMARKS

Claims 1-23 appear in this application for the Examiner's review and consideration. Claims 1, 3-6, 9-10, and 12-13 are amended and new Claim 23 is added herein. The amendments to the claims and the addition of new claim 23 are fully supported by the specification and original claims. No new matter has been added. Specifically, the amendments of Claims 1, 6, 9 and 12 to recite the step of recovering GMP by removing it

from the resin are supported in the specification at page 4, line 20, and by the examples. New claim 23 is supported by original claim 13.

Claims 1, 6, 9, and 12 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification as set forth on pages 2-3 of the Office Action. Applicants traverse.

Claims 1, 6, and 9, as amended, require the recovery of GMP from the resin. The claims as amended contain subject matter that is fully described in the specification, for example, at page 4, lines 20-21, and clearly set forth the Applicants' invention. Claim 12 presently requires "recovering of GMP as the retentate," which subject matter is also described in the specification. Applicants therefore request the Examiner withdraw the rejection under 35 U.S.C. §112, first paragraph.

Claims 1-13 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite, for the reasons set forth on pages 3-4, of the Office Action.

As stated above, Applicants herein have amended Claims 1, 6, and 9 to distinctly claim and set forth the process steps of their invention, resulting in the extraction of GMP.

Claim 12 presently requires the "recovering of GMP as the retentate" and distinctly sets forth the Applicants' invention. Applicants have amended Claim 13 to remove any possible confusion that may have existed.

Claims 3 and 4 have been amended so that the terms now have proper antecedent basis.

Claim 10 has been amended to more clearly set forth Applicants' invention. Claim 10 now recites the process according to claim 9 wherein the step of separating the resin from the treated liquid material is accomplished by filtration or centrifugation and the treated liquid material is dried by spray drying. The term "treated material" has been deleted.

Amended Claim 12 now claims the process according to claim 1, wherein the step of removing the GMP from the resin is accomplished by washing the resin with demineralized water; desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse; washing the resin with demineralized water; combining the eluate and the washings; demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and recovering the GMP as the retentate. Claim 12 now clearly and distinctly sets forth Applicants' invention.

The Examiner rejects Claims 4, 5 and 12 for requiring steps that are not required or suggested by Claim 1 and rejects Claim 10 for requiring steps that are not required or

suggested by Claim 9. In view of the amendments to Claims 4, 5, 10 and 12, Applicants believe that the claims further limit the independent claims from which they are dependent and are now in proper dependent from.

In view of the amendments and remarks above, Applicants, respectfully request that the Examiner withdraw the rejection of Claims 1-13 under 35 U.S.C. §112, second paragraph.

Claims 1-3 and 5-13 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,434,250 to Shimatani for the reasons set forth on pages 4-5 of the action. Applicants traverse.

Applicants invention is directed to a process for the extraction of GMP from lactic raw materials. One of the objectives of Applicants' invention is to recover purified GMP. The claimed process comprises the steps of:

> deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;
>
> contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;
>
> separating the resin from the treated liquid material; and
>
> recovering GMP by separating it from the resin.

In contrast, Shimatani discloses and claims a process for obtaining sialic acids. The objective of Shimatani's process is to produce sialic acid that can be added to breast milk and functional food. The process taught by Shimatani produces a sialic acid in a mixture composed of sialic acid-bound oligosaccharides, sialic acid-bound peptides and sialic acid bound lipids (Claim 1 and column 4, lines 8-11). In contrast, Applicants invention is designed to recover GMP (asialic or sialic) from lactic raw materials.

The desialylated derivatives of CGMP or GMP may be prepared in the art by subjecting the caseino-glycomacropeptide to a subsequent desialylation step, in which the oligosaccharide component of the glycomacropeptide is freed from sialic acids. To this end, the crude caseino-glycomacropeptide, which has not been purified beforehand by gel filtration, may be treated with an enzyme which specifically cleaves the sialic acid residues, e.g. a neuraminidase of Clostridium perfringens, after which the enzyme is thermally deactivated and the solution concentrated and dried, e.g. by freeze-drying. The sialic acid residues may advantageously be further cleaved by hydrolysis with a mineral acid in dilute

aqueous solution, e.g. hydrochloric or sulfuric acid. It is quite clear that the present method can not produce desialylated residues and it is not its objective. Furthermore, Shimatani does not teach the preparation of a protein component (as a treated liquid material) suitable for infant nutrition besides GMP.

The differences in objectives between the Applicants' and Shimatani's processes are further evident upon comparison of process steps. Shimatani's sialic acid removal process comprises the steps of (1) acidifying whey to a pH of 2-5; (2) contacting the acidified whey with a cation exchanger to produce exchanger-passed solution ("EPS"); and (3) concentrating and/or desalting the EPS. The process can further comprise of the steps of (4) drying the EPS; (5) desalting by the EPS by ultrafiltration; and/or (6) crystallizing the EPS to remove lactose.

Shimatani does not teach the combination of steps of Applicants' GMP extraction process. As noted above, present claim 1 is directed to a process for extracting GMP by deionizing lactic raw material and then contacting the deionized lactic raw material with an anionic resin to remove GMP from the deionized lactic raw material. The resin with the GMP thereon is separated from the treated liquid and GMP is then obtained by eluting it from the resin. Shimatani's process does not involve the steps of (1) contacting the deionized lactic raw material with an anionic resin, (2) separating the resin from the treated liquid material, or (3) removing the GMP from the anionic resin after separation of the resin from the treated liquid material. The Applicants' GMP extraction process and Shimatani's sialic acid recovery process are distinct as evidenced the different products extracted.

The Examiner further rejects, Claims 1-3 and 5-13 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,434,250 to Shimatani in view of Marshall (Ref. AL). Applicants traverse this rejection.

As discussed above, Shimatani fails to teach or suggest the steps of Applicants' GMP extraction process. Furthermore, Marshall also fails to teach the steps of Applicants' GMP extraction process as admitted by the Examiner. Finally, neither Shimatani nor Marshall combined or alone teach or suggest the Applicants' GMP extraction process. Therefore, the rejection of Claims 1-3 and 5-13 under 35 U.S.C. §103(a) should be withdrawn.

In view the foregoing remarks and amendments it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated. Should any issues remain, a personal or telephonic interview is respectfully requested to discuss the same in order to expedite the allowance of all the claims in this application.

No fees are believed to be due for the claim changes made in this response. Should any fees be due, please charge them to Winston & Strawn Deposit Account No. 501-814.

Respectfully submitted,

Date: 2/15/02

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## APPENDIX A - PRESENTLY PENDING CLAIMS

1. (Twice Amended) A process for the extraction of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

recovering GMP by separating it from the resin.

2. The process according to claim 1 wherein the lactic raw material is one of sweet whey obtained after separation of casein coagulated with rennet, a concentrate of sweet whey, a sweet whey or such a whey demineralized to by electrodialysis, ion exchange, reverse osmosis, electrodeionization or a combination of these procedures, a concentrate of sweet whey demineralized by electrodialysis, ion exchange, reverse osmosis, electrodeionization or a combination of these procedures, a concentrate of proteins of substantially lactose-free sweet whey obtained by ultrafiltration, followed by diafiltration (ultrafiltration with washing), mother liquors of the crystallization of lactose from sweet whey, a permeate of ultrafiltration of a sweet whey, the product of hydrolysis, by a protease, of a native casein obtained by acid precipitation of skimmed milk with an inorganic acid or by biological acidification, where appropriate with addition of calcium ions or alternatively of a micellar casein, obtained by microfiltration of a skimmed milk, the product of hydrolysis of a caseinate by a protease.

3. (Amended) The process according to claim 1 wherein the lactic raw material is sweet whey having a solids content of about 10 to 23 percent by weight.

4. (Amended) The process according to claim 1 wherein the lactic raw material is a liquid or a dispersion of solids in a liquid and which further comprises adding calcium ions to the lactic raw material after the deionizing step.

5. (Amended) The process according to claim 1, which further comprises the step of treating the resin with an alkaline material prior to contacting the substantially deionized lactic raw material with the resin.

6. (Twice Amended) A process for the extraction of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material, wherein the substantially deionized lactic raw material contacts the resin in a gently stirred reactor at a temperature of less than 50°C for one to ten hours to adsorb the GMP onto the resin;

separating the resin from the treated liquid material; and

recovering GMP by removing it from the resin.

7. The process according to claim 6 wherein the reactor is at a temperature between 0°C and 15°C and the resin is basic and in macroporous or macrocross-linked gel form.

8. The process according to claim 1 wherein the substantially deionized lactic raw material contacts the resin until the treated liquid material attains a constant pH of between about 4.5 to 5.5.

9. (Twice Amended) A process for the extraction and removal of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material;

concentrating the treated liquid material by evaporation and drying; and

recovering GMP by separating it from the resin.

10. (Amended) The process according to claim 9 wherein the step of separating the resin from the treated liquid material is accomplished by filtration or centrifugation and the treated liquid material is dried by spray drying.

11. (Amended) The process according to claim 1 wherein the anionic resin and the deionized lactic raw material are present in a ratio by volume of between 1:1 and 1:30.

12. (Amended) The process according to claim 1, wherein the step of removing the GMP from the resin is accomplished by washing the resin with demineralized water;

desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse;

washing the resin with demineralized water;

combining the eluate and the washings;

demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and

recovering the GMP as the retentate.

13. (Amended) The process according to claim 12 wherein the basic aqueous solution comprises NaOH, KOH or $Ca(OH)_2$, in a concentration of less than 8%.

14. (Amended) The process of claim 1 wherein the treated liquid material has an amino acid profile that is reduced in threonine and enriched in aromatic amino acids and tryptophan relative to the lactic raw material.

15. (Amended) The process of claim 14 wherein, relative to the lactic raw material, the threonine content is reduced by about 15 to 40%, and the aromatic amino acids and tryptophan are increased by about 20 to 60%.

16. (Amended) The process of claim 14, wherein the treated liquid material is included in an infant or dietetic product as protein raw material.

17. (Amended) The process of claim 9 wherein the treated liquid material is included in an infant or dietetic product as protein raw material.

18. (Amended) The process of claim 10 wherein the dried treated liquid material is included in an infant or dietetic product as protein raw material.

19. (Amended) The process of claim 1 wherein the GMP obtained therefrom includes less than 1% by weight of fat, less than 0.2% by weight of lactose, and less than 3% by weight of true whey products and is included with a carrier in a composition.

20. (Amended) The process of claim 19 wherein the composition is a pharmaceutical composition containing the GMP as an antithrombotic, antidiarrheal or antibacterial agents.

21. (Amended) The process of claim 19 wherein the composition is a food composition containing the GMP as an emulsifying, gelling or foaming agent.

22. (Amended) The process of claim 19 wherein the composition is a dental composition containing the GMP as an agent against plaque and caries.

23. (New) The process according to claim 12, further comprising the step of freeze-drying the retentate.

## APPENDIX B - MARKED COPY OF CLAIMS

1. (Twice Amended) A process for the extraction of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

[rinsing the resin to obtain the] recovering GMP by separating it [there]from the resin.

3. (Amended) The process according to claim 1 wherein the lactic raw material is sweet whey having[s] a solids content of about 10 to 23 percent by weight [and is completely deionized during the cation removal step].

4. (Amended) The process according to claim 1 wherein the lactic raw material is a liquid or a dispersion of solids in a liquid and which further comprises adding calcium ions to the lactic raw material after the deionizing [cation removal] step.

5. (Amended) The process according to claim 1, which further comprises the step of treating the resin with an alkaline material prior to contacting the substantially deionized lactic raw material with the resin.

6. (Twice Amended) A process for the extraction of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to

remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material, wherein the substantially deionized lactic raw material contacts the resin in a gently stirred reactor at a temperature of less than 50°C for one to ten hours to adsorb the GMP onto the resin;

separating the resin from the treated liquid material; and

[rinsing the resin to obtain the] recovering GMP by separating it [there]from the resin.

9. (Twice Amended) A process for the extraction and removal of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; [and]

concentrating the treated liquid material by evaporation and drying; and

recovering GMP by separating it from the resin.

10. (Amended) The process according to claim 9 wherein the step of separating the resin from the treated liquid material is accomplished by filtration or centrifugation and the treated liquid material is dried by spray drying [and which further comprises separating the resin from the treated material by filtration or centrifugation prior to evaporation and drying].

12. (Amended) The process according to claim 1, wherein the step of recovering the GMP from the resin is accomplished by [which further comprises the steps of:]

washing the resin [separating the GMP from the resin by washing the resin] with demineralized water [to obtain an eluate];

desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse;

washing the resin with demineralized water;

combining the eluate and the washings;

demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and

recovering the GMP as the retentate.

13. (Amended) The process according to claim 12 wherein[,] the basic aqueous solution comprises NaOH, KOH or $Ca(OH)_2$, in a concentration of less than 8% [wherein the retentate is freeze-dried to recover the GMP].

23. (New) The process according to claim 12, further comprising the step of freeze-drying the retentate.